Priapism is an emergency

CHAPTER 7

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Abstract

The term priapism describes erections of >4 hours that arise in the absence of or last well beyond sexual stimulation. Ischaemic priapism is the most common form and treatment success is strongly dependent on the duration of priapism. The aetiology is widely variable as a result of which several specialisms can be confronted with this condition. Over the past few years, urologists increasingly have to deal with patients who do not suffer from erectile dysfunction, but nevertheless use intracavernous injections with priapism as a result. These men are often reluctant to see a doctor due to shame and ignorance, which often leads to delayed treatment. According to current guidelines, early prosthesis implantation is recommended if the priapism lasted >36 hours. Treatment of stuttering priapism should be focused on prevention of subsequent episodes. Non-ischaemic priapism generally follows a mild course and can initially be approached conservatively.

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Ladies and Gentlemen,

Priapism is a pathological erection that lasts more than 4 hours and has potentially severe consequences. A distinction is made between the ischaemic, non-ischaemic and intermittent form. Priapism has various causes, so that not only urologists, but also other specialists –for example doctors on the emergency department, psychiatrists, neurologists, anaesthesiologists, doctors on the intensive care unit and cardiologists– may have to deal with this disorder. Clitoral priapism is not considered in this article.

Patient A, a 54-year-old healthy man visited his general practitioner, because of a painful erection that already lasted for more than 36 hours. The priapism occurred after he had injected 0.3 ml of papaverine 15 mg/phentolamine 0.5 mg in one of his corpora cavernosa (CC), even though he did not have erectile dysfunction. He had obtained this drug from a friend. Embarrassment and ignorance had prevented him from seeking medical help earlier. The general practitioner immediately referred the patient to the urology department of the nearest hospital. Blood gas analysis of blood that was aspirated from the CC showed values matching severe ischemia.

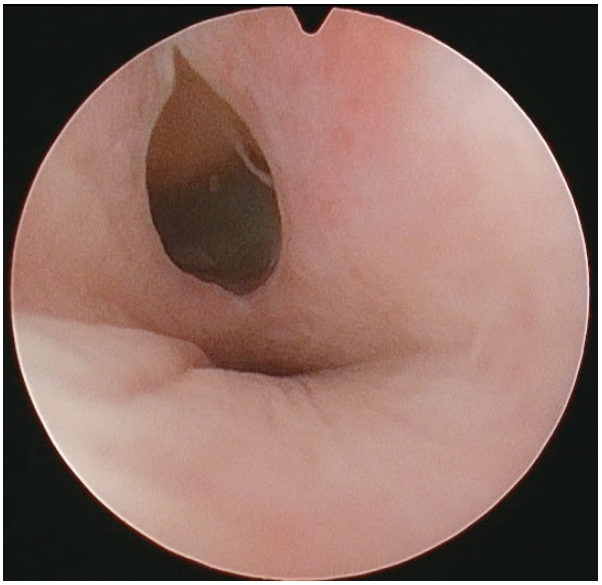

Figure 1. *Cystoscopic image of patient A with in the left upper quadrant a urethral fistula as a consequence of erosive damage that occurred after the placement of a penile prosthesis.*

To achieve definitive detumescence, repeated aspiration of dark coloured arterial blood from the CC was performed, followed by local administration of phenylephrine, without success. Because of the >36-hour duration of the priapism, shunt surgery was rejected. In the absence of other treatment options to prevent complete erectile dysfunction, the patient was referred to our centre for penile prosthesis implantation counselling, in the short term or after a period of months.

The patient opted for implantation of a semi-rigid penile prosthesis in the short term. The postoperative course was complicated by urethral erosion (Figure 1). Despite multiple re-interventions, we eventually had to explant the prosthesis.

Patient B was a 5-year-old boy visiting us with his parents because he suffered from a persistent erection. Twelve days earlier, he had fallen with his crotch on a radiator.
During the physical examination, we observed an ecchymosis left lateral to the penile base and swollen CC that were not painful to palpation. We performed a Doppler ultrasound of the penile vasculature and observed an increased arterial 'flow' centrally in the right corpus cavernosum on the penile-scrotal transition, originating from a tear in the a. profunda of the penis. Based on the clinical pattern and this result, we diagnosed the patient with "non- ischaemic" priapism, which we treated conservatively.
After 10 days the erection had disappeared. When we saw the patient 6 weeks after the trauma, the CC were perfectly pliant. The parents also observed "normal" penile erections again.

Patient C, a 23-year-old man, visited our outpatient clinic because he experienced frequent episodes of painful nocturnal erections disturbing his sleep. These nocturnal erections persisted for up to 4 hours before the penis spontaneously became flaccid. He was known with a medical history of homozygote sickle cell disease.
We diagnosed the patient with "intermittent priapism" and treated him with cyproterone acetate, which is an anti-androgenic drug, after which the priapism did not recur. Of course, it was necessary to check his serum testosterone levels regularly.

Discussion
Priapism is a rare condition. A Dutch study shows an annual incidence of priapism-related symptoms at the general practice of 1.5 per 100,000 persons. [1]

In the past 32 years, 85 patients were registered in the University Medical Center Groningen, who, in total, experienced 131 episodes of priapism. In 66 (77.6%) it concerned ischaemic priapism, in 9 (10.6%) non-ischaemic, in 7 (8.2%) intermittent priapism and in 3 (3.5%) no information on this subject could be found. The table describes the causes of the different forms of priapism in our patient population.

Ischemic priapism
Pathophysiology
In ischaemic priapism, also called "low-flow priapism", a compartment syndrome occurs, including high intracavernous pressures. This impedes venous outflow and secondarily the circulation, exposing the cavernous tissue to ischemia. [2] This form is therefore usually associated with pain.

Table 1. Aetiology of the different forms of priapism

Form	Cause	Remarks
ischemic (n=66)	intracavernous injection (n=37)	• papaverine/phentolamine (n=26) • papaverine (n=3) • alprostadil (n=2) • not specified (n=6)
	medication (n=14)	• antipsychotic (n=8) combined with SSRI (n=1) • alphablocker (n=1) • amphetamine (n=1) • heparine (n=1) • androgens (n=1) • vasodilatator (n=1)
	idiopathic (n=7)	
	sickle cell disease (n= 4)	
	segmental trombosis (n=4)	• right CC (n=1) • left proximal CC (n=2) • bilateral CC +CS , penile part (n=1)
non-ischemic (n=9)	trauma (n=5)	• perineal (n=3) • scrotal/penile (n=1) • iatrogenic (n=1)*
	neurogenic (n=2)	• spinal cord laesion C7 (n=1) • spinal cord laesion T3-4 (n=1)
	arterio-cavernous fistula eci	
intermittent (n=7)	sickel cell disease (n=3)	
	idiopathic (n=4)	
unknown (n=3)		

CC = corpus cavernosum, CS = corpus spongiosum; C7 = cervical 7; T3-4 = thoracic 3-4; SSRI = selective serotonin reuptake inhibitor

** After an earlier performed corporoglandular shunt for ischemic priapism.*

After 12-24 hours, the first irreversible histopathological changes occur. After 24-48 hours, the pathologists observe diffuse endothelial destruction. After 48 hours, necrosis develops with fibroblast-like transformation of the smooth muscle cells. [3] These rapidly occurring histopathological changes emphasise the urgency of timely treatment.

Aetiology
In our patient population, the most common cause of ischaemic priapism was the intracavernous injection of vasodilating agents (n=37). Increasingly, these illegally obtained injections with papaverine 15 mg/phentolamine 0.5 mg are used in a recreational setting, of whom patient A was an example. Especially in this group, we observed a longer patient delay (3.8 hours on average (SD: 13.9) against 15.2 hours (SD: 13.0) in the non-recreational users). After all, the latter group is extensively informed about the risks of and how to deal with priapism.

Besides the factors mentioned in Table 1, ischaemic priapism can be caused by neoplasms (metastatic or regional infiltration), substance abuse (e.g. cocaine, alcohol or marijuana), infections (toxin-mediated) and metabolic diseases (e.g. amyloidosis or gout).

Diagnostics
The diagnosis should be confirmed by gas analysis of blood aspirated from the CC. A Doppler ultrasound of the penile vasculature can also be performed, especially when drainage followed by injection of a sympathomimetic agent has not led to detumescence.

Treatment
Drainage and the local administration of phenylephrine were enough to achieve detumescence in 7.7% of our patients. The duration of priapism is an important predictor of success of this treatment. According to the most recent literature, this treatment is hardly effective in ischaemic priapism lasting more than 24-36 hours. Additional treatment should therefore preferably be performed within 24 hours after the occurrence of priapism. The second treatment step may consist of performing a surgically applied shunt between the CC and either the corpus spongiosum or the greater saphenous vein. From a recent series of 45 patients describing the application of the latest technique, the T-shunt with or without intracavernous snake tunnelling, it appeared that with this technique too, treatment success was strongly dependent on the duration of priapism. (7) If shunt surgery is performed <24 hours after the occurrence of priapism, the results are favourable. However, 50% of the successfully treated patients still developed erectile dysfunction. After >48 hours it was usually impossible to achieve detumescence let alone prevent erectile dysfunction.

In recent years, the discussion among experts has focused on the timing of implantation of a penile prosthesis in patients with refractory priapism. The European guideline states that shunt surgery should no longer be performed if the priapism persisted for more than 36 hours, but instead the patient should be counselled for early implantation of a penile prosthesis (<2 weeks after the occurrence of priapism). (4,6) An important advantage of early implantation is the possibility to preserve the penis' original length during erection. Figure 2 is a schematic illustration of a semi-rigid penile prosthesis.
However, placement of a penile prosthesis is not without risks, which also can be seen from the history of patient A. In this context, an MRI of the penis can probably play a role in the decision making and prevent overtreatment. The sensitivity of an MRI in indicating necrosis of the swelling tissue in the CC appeared to be 100%. (8) If there is hardly any necrosis to be seen on the MRI-scan, a more conservative approach is preferred.

Non-ischemic priapism

Non-ischaemic priapism (high-flow priapism) is usually caused by a blunt trauma in the crotch or perineal area but can also be a consequence of a disturbed neurological control, for example in patients with a high spinal cord lesion. Moreover, non-ischaemic priapism can occur after the treatment of ischaemic priapism due to iatrogenic needle damage to the deep artery of the penis. (4)

Diagnostics

The clinical presentation consists of a constant, non-painful and semi-tumescent erection, mostly occurring after a luxating moment, as was also the case in patient B. With doppler ultrasound an increased flow can be observed with pooling of blood in the CC. Gas analysis of blood from the CC is normally not necessary, but still often performed for medico-legal reasons.

Treatment

Since it concerns a non-ischaemic and non-painful form of priapism, a conservative approach is justified. (5,6) In our population, however, 2 of the 9 patients suffered from a persistent arterial-cavernous fistula with a pseudo-aneurysm, which could be treated successfully with selective embolisation.

Intermittent priapism

The intermittent (or "stuttering") form is characterised by frequently recurring episodes of ischaemic priapism and occurs mainly in patients with sickle cell disease, like patient C. The episodes most often begin during the night when sleep-related erections occur and are mostly self-limiting. Nonetheless, 33% of these patients experience progression to a persistent ischaemic priapism, for which they need treatment. (9) Within our population, this was the case in 5 of the 7 patients.

Pathophysiology

There is a possible molecular explanation for the pathogenesis of intermittent priapism, which is based on a disturbance in the nitric oxide pathway, caused by endothelial damage and the capture of nitric oxide in the CC by oxygen and haemoglobin that are released during haemolysis. (10,11) As a consequence, there is a reduced availability of nitric oxide in the CC, which causes a compensatory dysregulation of penile phosphodiesterase type 5 (PDE-5). The production of this enzyme is directly controlled by cyclic guanosine monophosphate (cGMP).
During an erectogenic stimulus, accumulation of cGMP in the smooth muscle tissue occurs, due to the decreased PDE-5 expression, resulting in uncontrolled vasodilatation.

Treatment

Both adequate treatment in the acute setting and preventative treatment are most important for this form of priapism. According to the international guidelines, anti-androgens and gonadotropin-releasing hormone (GnRH)-agonists should be the most effective to achieve this. (5,6) These drugs, however, have undesirable side effects, such as the inhibition of spermatogenesis and erectile dysfunction.

Both 5-α-reductase inhibitors and antifungals have proven to be effective in the prevention of priapism episodes. Nevertheless, we consider the prescription of these substances to be obsolete because of severe, irreversible, side effects.
Treatment with PDE-5 inhibitors has shown some positive results. This is probably due to the paradoxical effect of a slightly increased basal cGMP concentration in the CC, resulting in restoration of the PDE-5 expression and activity. (12)

Ladies and gentlemen, priapism is an emergency, for which direct reference to a hospital is necessary. The pathophysiology has only been partially clarified. The treatment of patients with refractory ischaemic priapism is particularly difficult. The role of MRI in treatment decision making in this group deserves further study.
When ischaemic priapism lasts >36 hours, early implantation of a penile prosthesis is recommended. This treatment is unfortunately associated with high complications risks, such as infection and prosthesis erosion. Implantation of a penile prosthesis in a later phase can be extremely difficult due to cavernous fibrosis, as a result of which the original length of the penis in erection can no longer be reached.
Recreational use of pro-erectile agents by intracavernous injection is problematic since it concerns a poorly informed group of patients in whom embarrassment plays an important role.

Keypoints

- A distinction is made between three forms of priapism: ischemic-, non-ischemic- and intermittent.
- Ischemic priapism is the most common form and results in severe erectile dysfunction if not treated timely
- When ischemic priapism lasts beyond 36 uur hours, early penile prothesis implantation (< 2 weeks after the occurrence of priapism) is recommended.
- The duration of ischemic priapism is an important predictor of treatment efficacy.
- MRI of the penis may play an important role in treatment decision making of priapism that exists >36 hours and thereby prevent overtreatment.
- The symptoms and consequences of non-ischemic are usually mild and invasive treatment is mostly not necessary.
- The treatment of intermittent priapism should primary be focused on prevention.
- Pro-erectile drugs are sometimes used recreationally, amongst others intracavernous injection; in these patients the delay is usually longer compared tot the well informed patients who are treated by a urologist.
- Adequate information and guidance are important when it concerns priapism patients; the high risk on development of permanent erectile dysfunction should always be discussed.

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